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REMARKS

Claims 134-146 are pending in the subject application. By this Amendment, applicant has canceled claims 137, 138, 144 and 145, and has amended claims 134, 135, 141 and 142. Accordingly, claims 134-136, 139-143 and 146 will be pending in the subject application upon entry of this Amendment.

In view of the arguments below, applicant maintains that the Examiner's rejections have been overcome, and respectfully request that they be withdrawn.

Rejections under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 134, 135, 137-142 and 144-146 under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification. Specifically, the Examiner alleges that applicant has only enabled one NADE protein.

In response, applicant respectfully traverses the Examiner's rejection.

The test for enablement is whether one skilled in the art could, at the time of the invention, make and use the claimed invention based on the disclosure and the information known in the art without undue experimentation. Applicant maintains that the claimed invention satisfies the test for enablement, and that the Examiner has not set forth sufficient grounds for concluding

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otherwise.

The subject invention encompasses methods of determining whether an agent affects apoptosis using the NADE proteins of the invention. As disclosed in the specification, NADE, or P75^{NTR}-Associated Cell Death Executor, represents a group of proteins that modulate apoptosis through interaction with the p75^{NTR} receptor. As the Examiner concedes, applicant has determined the specific regions of the NADE proteins required for interaction with the p75^{NTR} receptor. The instant specification discloses the residues of the NADE proteins which are required for binding to the p75^{NTR} receptor as well as working examples of the interaction between a NADE protein and a p75 neurotrophin receptor. The NADE protein in these examples is the isolated mouse NADE protein (SEQ ID NO:12), but the teaching of these examples extends to other NADE proteins, namely, but not limited to, NADE proteins comprising the amino acid sequence as set forth in SEQ ID NO:13, as well as SEQ ID NO:30-39. Furthermore, the specification discloses *inter alia* at page 55, lines 11-14 that "mapping studies revealed that NADE protein interacts with the cell death domain (amino acid residues 338-393) which is *identical* among mouse, rat and human." (Emphasis added) In addition, the specification discloses that NADE proteins are hydrophilic and acidic and possess, in addition to their binding site for the p75 neurotrophin receptor cell death domain (SEQ ID NO:1), two significant motifs: the leucine-rich nuclear export signal (NES) and ubiquitination sequences.

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Applicant maintains that one skilled in the art recognizes the significance of these residues of NADE in its interaction with the cell death domain of p75 as evidenced by, for example, Mukai, Jun et al. ("NADE, A p75^{NTR}-Associated Cell Death Executor, Is Involved In Signal Transduction Mediated BY The Common Neurotrophin Receptor p75^{NTR}", J. Bio. Chem. (2000) 275(23):17566-17570, submitted as Exhibit E with the March 8, 2001 Supplemental Information Disclosure Statement) which discloses on page 17569, paragraph 2 and Figure 2B, that the "C-terminal portion of NADE (amino acid residues 81-106) is necessary for the interaction with p75^{NTR}" cell death domain. Accordingly, applicant maintains that the specification provides one skilled in the art more than adequate disclosure, specifically the necessary attributes of the NADE proteins, in order use these proteins in the claimed methods without undue experimentation.

The Examiner also rejected claims 134-136 and 138-146 under 35 U.S.C. §112, first paragraph, as allegedly not enabled for the use of the claimed methods *in vivo*. With respect to claims 138, 144 and 145, applicant notes that these claims have been canceled rendering the rejection thereof moot.

In response to the rejection of claims 134, 135, 141 and 142, but without conceding the correctness of the Examiner's rejection, applicant notes that, as amended, claims 134, 135, 141 and 142, and their dependent claims, provide methods using NADE and p75^{NTR} *in vitro*, thereby obviating the rejection.

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The Examiner further rejected claims 134, 135, 137-142 and 144-146 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, was in possession of the claimed invention. Specifically, the Examiner asserts that the specification adequately describes only one NADE protein. With respect to claims 137, 138, 144 and 145, applicant notes that these claims have been canceled rendering the rejection thereof moot.

In response to the rejection of claims 134, 135, 139-142, and 146, applicant respectfully traverses the Examiner's rejection.

The test for written description under 35 U.S.C. §112, first paragraph, is whether the disclosure describes the claimed invention in sufficient detail so that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. According to M.P.E.P. §2163(I)(A), when evaluating whether support in the specification for the original claims is sufficient, "[t]here is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). The initial burden is therefore on the Examiner to present evidence of the lack of written description. Applicant maintains that the claimed

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invention satisfies the test for adequate written description, and that the Examiner has not set forth sufficient grounds for concluding otherwise.

Applicant contends that the NADE genus is disclosed in the specification as filed, adequately describing the NADE-specific features and providing numerous embodiments of its species. Applicant maintains that the specification adequately describes the characteristic attributes of the NADE genus. As mentioned above, the specification discloses that NADE proteins are hydrophilic and acidic and possess, in addition to their binding site for the p75 neurotrophin receptor cell death domain (SEQ ID NO:1), two significant motifs: the leucine-rich nuclear export signal (NES) and ubiquitination sequences. In addition, the specification discloses various species of human, mouse and rat NADE, as set forth in SEQ ID NOs:12-13 and SEQ ID NOs:30-39. (see page 16, line 36 to page 17, line 22 and page 53, lines 21-27 of the specification). Accordingly, applicant maintains that the disclosure as filed provides sufficient description of the NADE genus and its role in the regulation of p75^{NTR}-mediated apoptosis.

Moreover, according to M.P.E.P. §2163 (II)(A)(3)(a)(ii), the written description for a claimed genus may be satisfied by disclosure of relevant, identifying characteristics sufficient to show the applicant was in possession of the claimed genus. *Regents of the University of California v Eli Lilly*, 119 F3d. 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), cert. denied,

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523 U.S. 1089 (1998). Satisfactory disclosure depends on whether the necessary common attributes of the genus are recognized by one skilled in the art in view of the species disclosed. Applicant maintains that the claimed genus is supported by the disclosed species, and that the species disclose the necessary attributes of the claimed genus.

The Examiner also rejected claims 134-136 and 138-146 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement for the use of the claimed methods *in vivo*. With respect to claims 138, 144 and 145, applicant notes that these claims have been canceled rendering the rejection thereof moot.

In response to the rejection of claims 134, 135, 141 and 142, but without conceding the correctness of the Examiner's rejection, applicant notes that, as amended, claims 134, 135, 141 and 142, and their dependent claims, provide methods using NADE and p75^{NTR} *in vitro*, thereby obviating the rejection.

In view of the above remarks, applicant maintains that claims 134-146 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Summary

For the reasons set forth hereinabove, applicant respectfully requests that the Examiner reconsider and withdraw the

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rejections, and solicits allowance of the pending claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Commissioner for Patents
P.O. Box 1450 Alexandria, VA 22313-1450.

Alan J. Morrison
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7/7/04
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